

Claim 17, line 3, change "B27, B28" to --B27 and B28--.

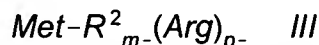
45
32 (Twice Amended) A process for the preparation of an insulin derivative or of a

physiologically tolerable salt thereof as claimed in claim 1, comprising [the construction of]

a) constructing a replicable, expression vehicle which contains a DNA sequence which codes for a precursor of the insulin derivative, in which the amino acid residue in position A1 of the A chain is linked to the amino acid residue B30 of the B chain via a peptide chain of the formula II



D₁ in which R^1_n is a peptide chain having n amino acid residues and n is an integer from 0 to 34, and the B chain is [prolonged in position B1 by] modified by covalent linkage of the amino acid at position B1 to a peptide chain of the formula III



in which R^2_m is a peptide chain having m amino acid residues, m is an integer from 0 to 40 and p is 0, 1 or 2,

b) [expression] expressing the DNA sequence which codes for a precursor of the insulin derivative in a host cell, and

c) [release of] releasing the insulin derivative from its precursor using chemical and/or enzymatic methods.

D2
~~50~~ 41. (Twice Amended) A precursor of [the] an insulin derivative, wherein the precursor has a sequence selected from the group consisting of SEQ ID NO.:11, SEQ ID NO.:6, SEQ ID NO.:8, and SEQ ID NO.:7 [as claimed in claim 63].

~~51~~ 42. (Twice Amended) [A] The precursor of claim ~~41~~ ⁵⁰, wherein the precursor has the sequence of SEQ ID NO.:6 [the insulin derivative as claimed in claim 64].

~~52~~ 43. (Twice Amended) [A] The precursor of claim ~~41~~ ⁵⁰, wherein the precursor has the sequence of SEQ ID NO.:8 [the insulin derivative as claimed in claim 65].

~~53~~ 44. (Twice Amended) [A] The precursor of claim ~~41~~ ⁵⁰, wherein the precursor has the sequence of SEQ ID NO.:7 [the insulin derivative as claimed in claim 66].

E
~~55~~ 45. (Amended) [A DNA] An isolated or purified nucleic acid comprising a sequence which codes for a precursor of [the] an insulin derivative having a sequence selected from SEQ ID NO.:11, SEQ ID NO.:6, SEQ ID NO.:8, and SEQ ID NO.:7 [as claimed in claim 41]. *the group consisting of*

D3
~~57~~ 46. (Amended) An expression vehicle comprising a [DNA sequence] nucleic acid as claimed in claim ~~45~~ ⁵⁶ [45].

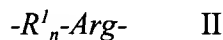
~~50~~⁶⁰ (Amended) An expression vehicle comprising a [DNA sequence] nucleic acid as claimed in claim ~~70~~⁵⁹ [46].

D3 ~~51~~⁶² (Amended) An expression vehicle comprising a [DNA sequence] nucleic acid as claimed in claim ~~71~~⁶¹ [47].

~~52~~⁶⁴ (Amended) An expression vehicle comprising a [DNA sequence] nucleic acid as claimed in claim ~~72~~⁶³ [48].

~~63~~³⁵ (Twice Amended) A process for the preparation of an insulin derivative as claimed in claim ~~70~~³³, comprising [the construction of]

D4 a) constructing a replicable, expression vehicle which contains a DNA sequence which codes for a precursor of the insulin derivative, in which the amino acid residue in position A1 of the A chain is linked to the amino acid residue B30 of the B chain via a peptide chain of the formula II



in which R^1_n is a peptide chain having n amino acid residues and n is an integer from 0 to 34, and the B chain is [prolonged in position B1 by] modified by covalent linkage of the amino acid at position B1 to a peptide chain of the formula III



LAW OFFICES

FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

in which R^2_m is a peptide chain having m amino acid residues, m is an integer from 0 to 40 and p is 0, 1 or 2,

b) [expression] expressing the DNA sequence which codes for a precursor of the insulin derivative in a host cell, and

c) [release of] releasing the insulin derivative from its precursor using chemical and/or enzymatic methods, wherein the precursor of the insulin derivative has the sequence

Met Ala Thr Thr Ser Thr Gly Asn Ser Ala Arg Phe Val Lys Gln

His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys

Gly Glu Arg Gly Phe Phe Tyr Thr Ile Lys Thr Arg Arg Glu Ala

Glu Asp Pro Gln Val Gly Gln Val Glu Leu Gly Gly Gly Pro Gly

Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys

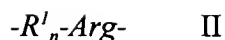
Arg Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr

Gln Leu Glu Asn Tyr Cys Asp

(SEQ ID No.: 11).

24
64: (Twice Amended) A process for the preparation of an insulin derivative as
23
claimed in claim 28, comprising [the construction of]

a) constructing a replicable expression vehicle which contains a DNA sequence which codes for a precursor of the insulin derivative, in which the amino acid residue in position A1 of the A chain is linked to the amino acid residue B30 of the B chain via a peptide chain of the formula II



in which R^1_n is a peptide chain having n amino acid residues and n is an integer from 0 to 34, and the B chain is [prolonged in position B1 by] modified by covalent linkage of the amino acid at position B1 to a peptide chain of the formula III



in which R^2_m is a peptide chain having m amino acid residues, m is an integer from 0 to 40 and p is 0, 1 or 2,

b) [expression] expressing the DNA sequence which codes for a precursor of the insulin derivative in a host cell, and

c) [release of] releasing the insulin derivative from its precursor using chemical and/or enzymatic methods, wherein the precursor of the insulin derivative has the sequence

Met Ala Thr Thr Ser Thr Gly Asn Ser Ala Arg

Phe Val Lys Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu

Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Glu Thr

Arg Arg Glu Ala Glu Asp Pro Gln Val Gly Gln Val Glu Leu Gly

Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly

Ser Leu Gln Lys Arg

Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln

Leu Glu Asn Tyr Cys Asn

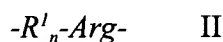
(SEQ ID NO.: 6).

LAW OFFICES

FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L. L. P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

32
31
(Twice Amended) A process for the preparation of an insulin derivative as claimed in claim 30, comprising [the construction of]

a) constructing a replicable expression vehicle which contains a DNA sequence which codes for a precursor of the insulin derivative, in which the amino acid residue in position A1 of the A chain is linked to the amino acid residue B30 of the B chain via a peptide chain of the formula II



in which R^1_n is a peptide chain having n amino acid residues and n is an integer from 0 to 34, and the B chain is [prolonged in position B1 by] modified by covalent linkage of the amino acid at position B1 to a peptide chain of the formula III



in which R^2_m is a peptide chain having m amino acid residues, m is an integer from 0 to 40 and p is 0, 1 or 2,

b) [expression] expressing the DNA sequence which codes for a precursor of the insulin derivative in a host cell, and

c) [release of] releasing the insulin derivative from its precursor using chemical and/or enzymatic methods, wherein the precursor of the insulin derivative has the sequence

Met Ala Thr Thr Ser Thr Gly Asn Ser Ala Arg

Phe Val Lys Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu

Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Ile Pro Lys Thr

Arg Arg Glu Ala Glu Asp Pro Gln Val Gly Gln Val Glu Leu Gly

LAW OFFICES

FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly

Ser Leu Gln Lys Arg

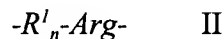
Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln

Leu Glu Asn Tyr Cys Asn

(SEQ ID NO.: 8).

29
28
36. (Twice Amended) A process for the preparation of an insulin derivative as
claimed in claim 31, comprising [the construction of]

174
a) constructing a replicable expression vehicle which contains a DNA sequence which
codes for a precursor of the insulin derivative, in which the amino acid residue in position A1 of
the A chain is linked to the amino acid residue B30 of the B chain via a peptide chain of the
formula II



in which R'_n is a peptide chain having n amino acid residues and n is an integer from 0 to 34, and
the B chain is [prolonged in position B1 by] modified by covalent linkage of the amino acid at
position B1 to a peptide chain of the formula III



in which R^2_m is a peptide chain having m amino acid residues, m is an integer from 0 to 40 and p
is 0, 1 or 2,

b) [expression] expressing the DNA sequence which codes for a precursor of the insulin
derivative in a host cell, and

LAW OFFICES

FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

54

D'

c) [release of] releasing the insulin derivative from its precursor using chemical and/or enzymatic methods, wherein the precursor of the insulin derivative has the sequence

Met Ala Thr Thr Ser Thr Gly Asn Ser Ala Arg

Phe Val Lys Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu

Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Ile Lys Thr

Arg Arg Glu Ala Glu Asp Pro Gln Val Gly Gln Val Glu Leu Gly

Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly

Ser Leu Gln Lys Arg

Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln

Leu Glu Asn Tyr Cys Asn

(SEQ ID NO.: 7).

Please add new claims 68-72 as follows:

-- ⁵⁴~~68~~. The precursor of claim ⁵⁰~~41~~, wherein the precursor has the sequence of SEQ ID NO.:11.

⁵⁶~~69~~. The isolated or purified nucleic acid of claim ⁵⁵~~45~~, having the sequence of SEQ ID NO.11.

⁵⁹~~70~~. The isolated or purified nucleic acid of claim ⁵⁵~~45~~, having the sequence of SEQ ID NO.:6.

LAW OFFICES

FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000